## **Contents**

Paı	rt I Epigenetic Alterations in Hypoxia	
1	Epigenetic Mechanisms as an Interface Between the Environment and Genome  Zdenko Herceg	3
2	Developmental Origins of Hypoxic Pulmonary Hypertension and Systemic Vascular Dysfunction: Evidence from Humans	17
3	Acquired Mitochondrial Abnormalities, Including Epigenetic Inhibition of Superoxide Dismutase 2, in Pulmonary Hypertension and Cancer: Therapeutic Implications	29
4	Epigenetics in Cardiovascular Regulation.  Claudio Sartori, Stefano F. Rimoldi, Emrush Rexhaj, Yves Allemann, and Urs Scherrer	55
Par	t II Hypoxia and High Altitude Residents	
5	Why Are High-Altitude Natives So Strong at Altitude? Maximal Oxygen Transport to the Muscle Cell in Altitude Natives	55
6	Novel Insights into Cardiovascular Regulation in Patients with Chronic Mountain Sickness  Stefano F. Rimoldi, Emrush Rexhaj, Mercedes Villena, Carlos Salinas Salmon, Yves Allemann, Urs Scherrer, and Claudio Sartori	3
7	Why Are High Altitude Natives So Strong at High Altitude? Nature vs. Nurture: Genetic Factors vs. Growth and Development 10 Tom Brutsaert	1

8	Functional Genomic Insights into Regulatory Mechanisms of High-Altitude Adaptation	113
	Jay F. Storz and Zachary A. Cheviron	
Par	t III Hypoxia and the Brain	
9	Influence of Hypoxia on Cerebral Blood Flow Regulation in Humans	131
	Craig D. Steinback and Marc J. Poulin	1 45
10	Imaging the Respiratory Effects of Opioids in the Human Brain Kyle T.S. Pattinson and Richard G. Wise	145
11	Regional Cerebrovascular Responses to Hypercapnia and Hypoxia Douglas R. Corfield and Leanne C. McKay	157
12	Implications of Oxygen Homeostasis for Tumor Biology and Treatment  Boyan K. Garvalov and Till Acker	169
13	Hyperoxia and Functional MRI  Daniel Bulte	187
14	Astrocytes and Brain Hypoxia  Nephtali Marina, Vitaliy Kasymov, Gareth L. Ackland, Sergey Kasparov, and Alexander V. Gourine	201
15	Bidirectional Control of Blood Flow by Astrocytes: A Role for Tissue Oxygen and Other Metabolic Factors Grant R.J. Gordon, Clare Howarth, and Brian A. MacVicar	209
16	Hypoxic Adaptation in the Nervous System: Promise for Novel Therapeutics for Acute and Chronic Neurodegeneration Rachel Speer and Rajiv R. Ratan	221
Pa	rt IV Molecular Oxygen Sensing	
17	Optical Analysis of Hypoxia Inducible Factor (HIF)-1 Complex Assembly: Imaging of Cellular Oxygen Sensing	247
18	Modulation of the Hypoxic Response  Christopher W. Pugh	259
Pa	rt V Physiological Responses to Hypoxia	
19	Central Sleep Apnea at High Altitude Keith R. Burgess and Philip N. Ainslie	275

Contents

20	Multigenerational Effects of Rearing Atmospheric Oxygen Level on the Tracheal Dimensions and Diffusing Capacities of Pupal and Adult Drosophila melanogaster	285
21	Hypoxia and Its Acid-Base Consequences: From Mountains to Malignancy  Erik R. Swenson	301
22	Ensemble Input of Group III/IV Muscle Afferents to CNS: A Limiting Factor of Central Motor Drive During Endurance Exercise from Normoxia to Moderate Hypoxia  Markus Amann and Jerome A. Dempsey	325
23	Physiological and Clinical Implications of Adrenergic Pathways at High Altitude  Jean-Paul Richalet	343
24	Hemoglobin Mass and Aerobic Performance at Moderate Altitude in Elite Athletes  Jon Peter Wehrlin, Bernard Marti, and Jostein Hallén	357
25	Does the Sympathetic Nervous System Adapt to Chronic Altitude Exposure?  Mikael Sander	375
26	Integrative Conductance of Oxygen During Exercise at Altitude  José A.L. Calbet, Carsten Lundby, and Robert Boushel	395
27	Modeling Variable Phanerozoic Oxygen Effects on Physiology and Evolution	409
28	Caudwell Xtreme Everest: An Overview  Michael P.W. Grocott, D.Z.H. Levett, D.S. Martin, M.H. Wilson, A. Mackenney, S. Dhillon, H.E. Montgomery, M.G. Mythen, and K. Mitchell	427
29	Energy Flux, Lactate Shuttling, Mitochondrial Dynamics, and Hypoxia	439
30	Everest Physiology Pre-2008	457
Abs	stracts from Hypoxia 2009-2015	465
Ind	ex	763